Coexistence of short and long term memory in a model network of realistic neurons

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Abstract

NMDA-mediated synaptic currents are believed to influence LTP. A recent model (Lisman et al., Nature Neurosci. (1993) 273–275) demonstrates that they can instead support short term memory based on rhythmic spike activity. We examine this effect in a more realistic model that uses two-compartment neurons experiencing fatigue and also includes long-term memory by synaptic LTP. We find that the network does support both modes of operation without any parameter changes, but depending on the input patterns. Short term memory functionality might facilitate Hebbian learning through LTP by holding a new pattern while synaptic potentiation occurs. We also find that susceptibility of the short term memory against new input is time-dependent and reaches a maximum around the time constant of neuronal fatigue (200–400 ms). This corresponds well to the time scale of the syllabic rhythm and various psychophysical phenomena. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

The NMDA class of glutamate receptors are commonly associated with the induction of synaptic long-term potentiation (LTP) and thus with a mechanism for long-term memory. Lisman et al. [3] recently suggested that NMDA-activated synaptic currents might also serve an entirely different purpose by supporting dynamic short term memory: The characteristic of NMDA-activated currents induces a neuronal bistability that allows for the persistence of an afferently stimulated spatial pattern without requiring any kind of synaptic structure.

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The study of Lisman et al. presents an original idea but also has three obvious drawbacks: (A) Such a short term memory has to coexist with long-term memory formed by LTP plasticity of the NMDA synapses. It is necessary to study the function of an NMDA-based short term memory in a network with structured synaptic weights, e.g. formed by Hebbian learning. Our approach is guided by the idea that cortical columns with their comparatively high internal connectivity are candidates for associative memories [1,6]. (B) The model neuron used in [3] is relatively simple as it considers only spike-generating and synaptic currents; in particular, it lacks slowly activating potassium channels to model neuronal fatigue or adaptation. Therefore, we employ a different neuron model presented by Pinsky and Rinzel [4] that does experience fatigue. (C) The study by Lisman et al. only investigates the mechanism for an NMDA-based dynamic short term memory but does not address its systematic functional, i.e. computational evaluation. Here we investigate the effect they describe under a more functional paradigm.

2. Methods

We simulate a network of 100 two-compartment neurons [4] each comprising two compartments with altogether five active and two synaptic currents controlled by eight independent variables. It has been derived from a 19-compartment model [5] by pooling fast spike generating currents into a somatic and slower, e.g. calcium-mediated ones into a dendritic compartment. We modeled all active and synaptic currents as in [4], with the exception of the AMPA-activated ones that have to be disabled as in [3] in order to give raise to the NMDA-effect. This adjustment is necessary to obtain short term memory capability.

The network is fully connected with a binary matrix of recurrent synapses; patterns are stored autoassociatively via clipped Hebbian learning. The matrix contains 38 binary patterns with activity $k = 10$, resulting in 30% matrix load; experiments with a complete matrix were performed for comparison. Each neuron can receive afferent input; the addressing pulse lasts 35 ms and is modulated by a poisson process with rate 0.5. Network activity is controlled by a graded inhibition modeling the activity in a pool of interneurons. The firing rate in this pool can be calibrated using the variable ϑ that represents the interneurons' firing threshold. We investigate the influence of ϑ variation on memory performance.

For evaluation of short term memory performance, we use an information theoretical distance measure called *quality* that is defined as the transinformation between an addressed pattern and network activity, normalized by the information content in one memory pattern. To measure the pattern completion achieved by associative retrieval, the quality *gain* between each address pattern and the resulting network activity is computed.

3. Results

Fig. 1 shows a raster plot of the network activity maintaining a pattern of 15 neurons that continues firing after input withdrawal. Even though all active cells
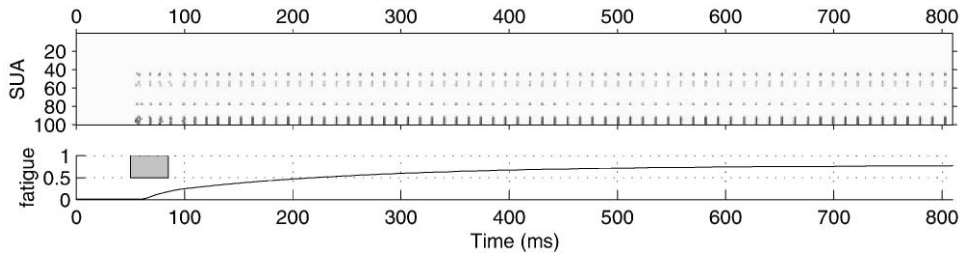
Fig. 1. Raster plot showing the persistence of an afferently excited pattern as single unit activity (above) and the trace of the fatigue variable of an active neuron (below) with its time constant of about 250 ms. Afferent input (symbolized by the shaded box) lasts 35 ms. Spike frequency is in the high gamma range around 80 Hz. In this experiment, the network is operating in a parameter regime where it maintains the pattern until a new stimulus is presented.

experience increasing fatigue and thus remain transient during the first 500 ms, the pattern persists longer than that. Persistence of the pattern relies on the NMDA-effect and does *not* have to be supported by synaptic structure. However, it does depend on some form of diffuse synaptic feedback because an isolated neuron would not be able to sustain stable firing.

We were able to operate the network in a parameter regime where spike frequency is in the upper range of the experimentally observed γ-band (around 80 Hz) whereas in [3], the effect was demonstrated at roughly 160 Hz.

Depending on maximal synaptic conductances g_{NMDA} and g_{GABA}, the network behaves differently with respect to maintaining input patterns: Higher conductances enable activity patterns to persist for arbitrarily long periods of time. In this case, the pattern continues after even the slow fatigue variable has become intransient as in Fig. 1 (the network will, however, switch to another input pattern quickly if one is presented). Lower conductances, on the other hand, allow for fatigue-induced network effects to interrupt the regularly firing pattern after several hundred milliseconds.

Fig. 2 shows the effect of using a connection matrix with autoassociatively stored patterns instead of an unstructured one: The network retains most of its capability to maintain arbitrary input patterns. For weak inhibition and small patterns (lower right), there is even some improvement although the matrix' structure does not support any of the patterns presented in these experiments.

The firing threshold ϑ of the interneuron pool provides a mechanism for selection of the pattern activity to be maintained: Lower thresholds cause stronger inhibition that allow fewer neurons to fire regularly. Stable pattern sizes depend linearly on ϑ; the variable ϑ might thus serve as a parameter for externally tuning the network to a specific pattern activity. Such tuning could be controlled by a suitable forward-inhibition mechanism that adapts the inhibition to fit pattern size.

When the network operates in a parameter regime where fatigue-induced termination of maintained patterns occurs, susceptibility to new stimuli is time dependent with a maximum at 200–400 ms: As the pattern persists, the network becomes more
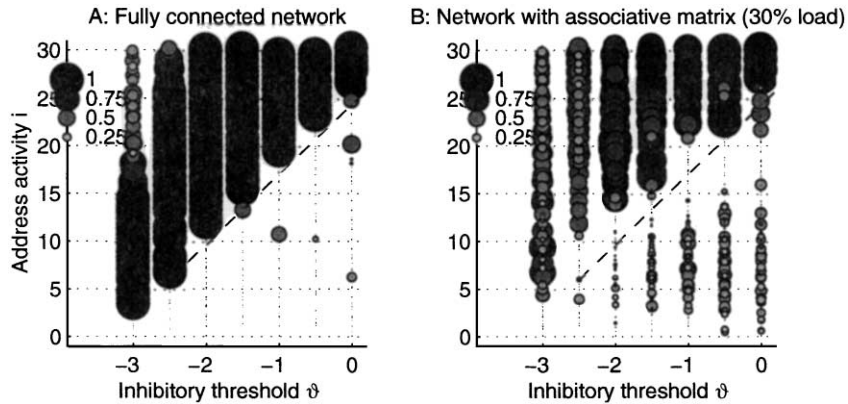
Fig. 2. Quality between input and activity, maintained for at least 400 ms after input withdrawal, measured on a fully connected network (left) and one loaded with 38 patterns comprising ten randomly selected ones, resulting in 30% matrix load (right). Input is presented to $i = 1$–30 neurons (vertical axes) as a 35 ms rectangular pulse modulated by Poisson-like noise, input patterns were random in both cases. Parameter settings allowed indefinite persistence of patterns. Horizontal axes show the interneuron's firing threshold ϑ. Each marker (●) represents the value of a quality maximum at least 400 ms wide during one experiment; darker, larger circles symbolize higher quality. The dashed line represents a sharp border between excellent and inferior short-term memory capability in figure A. Transition to a structured connection matrix shifts this border to greater activity but preserves most of the grid area featuring good memory.

sensitive to afferent input until, between 200 and 400 ms, very weak input suffices to switch the network to the new pattern. After that, the network develops a new, random pattern of suitable activity (depending on ϑ) that is again sustained for a similar period of time.

When the memory is addressed not with random input but with parts of stored patterns that are to be completed, i.e., when it is operated as a long-term memory, it has to solve a completely different task. Fig. 3 shows that although the network has been tuned to facilitate persistence and thus short term memory, it still has considerable completion capability. Not surprisingly, positive gain is concentrated in those areas of the $(\vartheta \times i)$-grid where the network does not maintain patterns well. Depending on the strength of synaptic coupling, it performs well either completing partially presented patterns (A), or filtering patterns distorted with spurious ones (B).

Optimization for short term memory tasks has side effects that impair the network's performance as an associative memory. Because the NMDA receptor occupancy S_{NMDA} saturates, different excitatory input cannot distinguish one neuron from another once they have both reached saturation. Thus for associative operation, the required discrimination between 'correct' and 'spurious' neurons must occur during the initial phase with still-increasing S_{NMDA} and has to be mediated by suitable coupling strengths that influence the S_{NMDA} grow rate. Forfeiting the short term memory capability and thereby regaining the AMPA-mediated currents' influence would yield significantly better pattern completion as in [6].
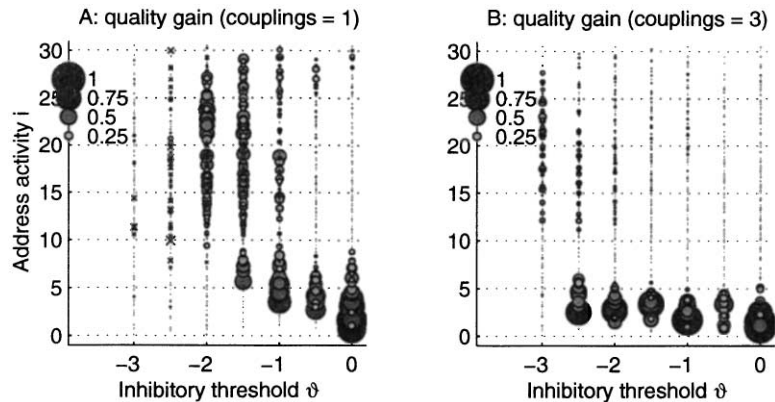
Fig. 3. Quality gain by associative retrieval; the plot shows maxima that have at least 20 ms duration. Darker, larger circles symbolize higher gain. The network was loaded with 38 patterns of activity $k = 10$; addressing occurred with incomplete patterns and patterns superimposed with spurious ones. (A) shows that with weaker coupling, considerable quality gain is achieved for large addresses from which the pattern was filtered. Conversely, (B) shows that for stronger coupling gain was mainly achieved by actual completion of small adresses. For intermediate coupling strengths (not shown) the memory undergoes a gradual shift of positive gain between the respective grid areas.

4. Conclusion

We showed that dynamic NMDA-based short term memory as proposed in [3] and associative memory using Hebb synapses can coexist in the same network of realistically modeled neurons. Of course, maintaining and completing patterns are mutually exclusive tasks and thus occur in disjoint parts of the inhibition/stimulus space. Both types of operation might also coexist in a cortical column. Such a coexistence could even play an important functional role provided that holding a pattern dynamically in short term memory would enable physiologically slow LTP processes to engrave that pattern in synaptic structure (and thus long term memory) by Hebbian learning. As NMDA-activated currents are in fact believed to participate in LTP, this idea provides an elegant functional interpretation of the role of NMDA channels.

Variation of the inhibition threshold ϑ by external activity as explored in our study is more relevant with respect to fast processes than varying the inhibitory synapses' GABA-conductance as in [3] since the latter would have to be effected by changes in transmitter concentration.

Also, we were able to show that fatigue, as implemented in the model we use, does not necessarily impede prolonged autonomous sustainment of an activity pattern. However, there is a parameter range, where this neuronal adaptation induces time-dependent network sensitivity to afferent input. Weak stimuli are most likely to switch the network to a new pattern if applied 200–400 ms after onset of the previous pattern. This time constant is known to play an important role in many aspects of behaviour and perception [2]. Examples of such processes include (i) the syllabic rhythm,

(ii) motor actions (e.g. "fast movements" of the arm), (iii) visual backward masking that is most evident if stimuli occur with a 200 ms delay, and (iv) the Lee effect, i.e. disturbance of speach production through delayed acoustic feedback being maximal when the delay is 200 ms.

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